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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,783	05/02/2002	John C. Herr	00415-03	8483

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UNIVERSITY OF VIRGINIA PATENT FOUNDATION
1224 WEST MAIN STREET, SUITE 1-110
CHARLOTTESVILLE, VA 22903

EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,783	HERR ET AL.	
	Examiner	Art Unit	
	James L Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,9-19,33-36 and 38-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,9-19,33-36 and 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

The amendment filed 17 March 2004 is acknowledged and has been entered. Claims 38-42 are newly added. Claims 4, 8, 20-32, and 37 have been cancelled. Claims 1-3, 5-7, 9-19, 33-36, and 38-42 remain in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The specification is objected to and claims 5, 6, 13, 14, and 41 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons of record that applicant provides insufficient written description and guidance for how one uses the conjugates as claimed.

Applicant's arguments filed 17 March 2004 have been fully considered but they are not deemed to be persuasive. Applicant urges that compositions, not methods of using the compositions are claimed, and that the conjugate compositions may have various diagnostic and contraceptive uses. This is not found persuasive for the reasons of record that one would not readily know for what condition a conjugate of a sperm-specific antibody with toxins, microbicides, or virucides would predictably function, other than delivery of a spermicidal toxin, in the absence of further description and guidance from applicant. Notwithstanding applicant's assertions to the contrary, a mere statement that a particular composition is part of the invention

in the absence of any description and guidance for how that composition is predictably used does not satisfy the requirements of 35 U.S.C. § 112, first paragraph.

Claims 1-3, 7, 9-12, 15-19, 33-36, 39, 40, and 42 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Herr et al. (US 5,830,472) in view of Owens et al. (J. Immunol. Meth. 168: 149, 1994) and Bird et al. (Science 242: 423, 1988) for reasons similar to those of record in the prior rejection of the similar subject matter of the prior claims.

Herr et al. (US 5,830,472) teach the S19 monoclonal antibody, produced by the hybridoma deposited as ATCC HB12144, and the use of the antibody as a spermicide or diagnostic. The reference teaches that, using the sequence of the antibody, conventional techniques can be employed to provide recombinant antibodies (see e.g. column 9, lines 3-7) and that the goals of the invention are met through the use of a humanized recombinant version of the monoclonal antibody (see e.g. col. 3, lines 12-24). The reference discloses methods for the isolation and sequencing of the variable regions of the heavy and light chains of the antibody from the hybridoma cell line and reports what were determined to be the genomic sequences of the cloned chains. Although the instant specification teaches that the light chain sequence disclosed in the reference contained errors, the sequences of the antibody chains produced by the deposited hybridoma and clonable from the teachings of the reference are a property thereof possessed and readily obtainable by one in possession of the deposited cell line or cloned

antibody-encoding sequences thereof. In contrast to the invention as instantly claimed, the reference does not specifically teach single chain Fv antibody fragments.

Owens et al. (J. Immunol. Meth. 168: 149, 1994) teach conventional techniques for genetic engineering of monoclonal antibodies for a variety of benefits, including to provide a more stable, higher-yield, and/or lower cost production means for the monoclonal antibodies than hybridomas. For example the production of single chain Fv fragments, wherein the variable regions of the heavy and light chains are linked together in a single polypeptide with a linker such as oligomers of (Gly_4Ser), is taught for use in conjugates with enzymes or drugs (see e.g. pages 155-156).

Bird et al. teach production of single chain Fv fragments for a variety of benefits, particularly in clinical applications. Benefits such as reduction of background non-specific binding for imaging or delivery purposes, reduced immunogenicity, rapid clearance, or better penetration due to elimination of constant regions of antibodies are taught (see e.g. page 426, col. 1). The reference confidently predicted that active single-chain antigen-binding proteins could be produced from the sequence of any monoclonal antibody (see e.g. page 425, col. 3).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have recombinantly engineered the S19 monoclonal antibody of Herr et al. using the conventional techniques and constructs as taught by Owens et al. or Bird et al. motivated by the direct suggestion in Herr et al. to do so and by the benefits taught by Owens et al. and Bird et al. to provide a more stable, higher-yield, and/or lower cost production means for

the monoclonal antibodies than hybridomas and to provide antigen-binding reagents for clinical applications with lower background non-specific binding, reduced immunogenicity, rapid clearance, or better penetration. One in possession of the deposited hybridoma of Herr et al. would have been in obvious possession of the sequences encoding the S19 monoclonal antibody for the recombinant engineering of the S19 monoclonal antibody. One would have had a more than reasonable expectation of success in view of the expectation of Bird et al., even in 1988, that single chain antibodies could be produced from any given monoclonal antibody. It would have been further obvious to have optimized the length of the conventional oligomeric linker within the known range for such linkers taught in, for example, Owens et al.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Herr et al. in view of Owens et al. and Bird et al. as applied to claims 1-3, 7, 9-12, 15-19, 33-36, 39, 40, and 42 above, and further in view of Russell et al. (U.S. Pat. No. 6,080,560).

The teachings of Herr et al. in view of Owens et al. and Bird et al. are as set forth above and differ from the invention as is now claimed by not specifically teaching producing the single chain antibodies in a plant host cell.

Russell et al. is cited to provide evidence that plant cells were well known in the art for the production of single-chain antibodies, such as those taught in Bird et al., for the benefits taught therein.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have used plant cells for the host cell for the cloning of the recombinant S19 antibodies taught by the combination of Herr et al. with Owens et al. and Bird et al. because Russell et al. teach plant cells for the production of such antibodies and one of ordinary skill would have been motivated to select any of the conventional host cells for the production of such antibodies with an extremely reasonable expectation of success. One would have been motivated to specifically select plant host cells for the benefits taught in Russell et al.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Applicant's arguments filed 17 March 2004 have been fully considered but they are not deemed to be persuasive in view of the new ground(s) of rejection.

Applicant urges that the making of a recombinant antibody is merely obvious to try. This is not found persuasive for the reasons of record, particularly in view of the teaching in Herr et al. to clone a humanized recombinant S19 antibody to meet the goals of the invention taught therein and in view of the conventional and predictable production of single chain antibodies, particularly for clinical applications such as in delivery conjugates, taught by Owens et al. and

Bird et al. Applicant urges that several examples in Owens et al. teach away from the use of single chain antibodies. This is not found persuasive for the reasons of record in view of the benefits taught for the use of single chain antibodies for clinical applications in particular. Applicant urges that the sequences of Herr et al. are not those as taught in the instant application. This is not found persuasive for the reasons of record because the reference of Herr et al. teaches the S19 monoclonal antibody which has, and is encoded in the deposited hybridoma by, sequences identical to those as instantly claimed. One in possession of the deposited hybridoma and, regardless of the published sequence in the reference, guided by the teachings of the combined references and their conventional methodologies would have isolated and cloned those encoding sequences from the hybridoma as desired by Herr et al. having sequences identical to those as instantly claimed. Notwithstanding applicant's argument to the contrary, one guided by the teachings of the references and in possession of an isolated molecule need not know the complete correct sequence of that molecule to be in obvious possession of that isolated molecule. Sequencing an old molecule does not make the molecule new or different from itself.

Applicant urges that the formation of multimers of the S19 single chain antibodies was an unexpected result. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., multimeric single chain antibodies) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, the

specification indicates that multimeric single chain antibodies were known to the art and were therefore not totally unexpected (see e.g. page 24).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

James L. Grun, Ph.D.
June 8, 2004

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641